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Gamma Probe Detection of Ectopic Parathyroid Adenoma

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A 34-year-old man with hypercalcemia had a sestamibi scan that showed increased uptake that appeared to correspond with a 7 mm density in the mediastinum, adjacent to the aortic arch, on chest CT. This lesion was thought to be consistent with an ectopic parathyroid adenoma. Prior to surgical exploration, the patient was injected intravenously with 12.3 millicuries of Tc99m-sestamibi. The lesion identified preoperatively did not show abnormal radionuclide uptake using the intraoperative gamma probe, and was subsequently determined to be a hyperplastic lymph node. However, abnormal activity was localized to the thymus gland, from which an ectopic parathyroid adenoma was successfully excised. The patient recovered without incident. The use of the intraoperative gamma probe was critical in identifying and resecting the ectopic parathyroid adenoma in this patient, and in general, may reduce surgical time and reduce the morbidity and/or complications associated with surgical exploration.

Introduction

The traditional approach to treating patients with primary hyperparathyroidism involved bilateral neck exploration with the goal of visualizing all four parathyroid glands and removal of the enlarged glands [1]. Although this approach was quite successful, there was always a chance of missing an ectopic parathyroid gland or being unable to

locate one of the four parathyroid glands. This concept has led to the development of the use of the gamma probe for intraoperative localization of parathyroid adenomas.

Primary hyperparathyroidism caused by a solitary adenoma accounts for over 80% of cases. During embryogenesis, the upper and lower parathyroid glands descend into the neck and, as a result, 20% of parathyroid glands are found in ectopic locations [2]. Most ectopic glands are found in close proximity to the thymus with the inferior parathyroid glands originating from the third bronchial pouch with the thymus [3].

Patients with hyperparathyroidism are frequently asymptomatic, detected only by screening. However, some patients may experience renal stones, polyuria, hypertension, constipation, fatigue, and mental status changes. Laboratory findings include an elevated serum and urine calcium, high urine phosphate with low to normal serum phosphate, normal to elevated alkaline phosphatase, and elevated parathyroid hormone [4].

Parathyroid glands larger than 1.5 cm are typically

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Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; SPECT, single photon emission computed tomography; VATS, video-assisted thoracoscopic surgery

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seen by computerized tomography scans, however smaller sized glands are difficult to identify. Without preoperative localization, reports have noted 33%–44% inability rates to identify glands by sternotomy [3]. While more than 95% of patients undergoing an initial surgical exploration are cured of their disease, patients with persistent or recurrent hyperparathyroidism often need further diagnostic imaging to detect these residual ectopic parathyroid glands [2].

Video-assisted thoracic surgery (VATS) and three dimensional-CT imaging in conjunction with radionuclide imaging have been used in localizing parathyroid glands and aiding in surgical planning. Not only did VATS allow better visualization than the open cervical approach but the cervical approach with median sternotomy led to postoperative complications such as pleural effusions, pneumothorax, and anterior mediastinitis [5]. Thus, pre-operative localization is still important in addition to direct visualization as 25% of primary hyperparathyroidism is caused by ectopic mediastinal parathyroid glands, with 2% of these not accessible to standard cervical approaches [6].

SPECT/CT has also been utilized in imaging parathyroid adenomas. SPECT/CT may provide value in locating ectopic parathyroid adenomas but does not add value in locating a normally located parathyroid adenoma or hyperplasia. Thus, by eliminating the CT portion of the study, imaging time and radiation exposure to the patient

are reduced [7]. However, dual phase imaging which includes two sets of images, one at 5–15 minutes (early) and one at 2–3 hours (delayed) has been found to be far superior than single-phase imaging and therefore, early SPECT/CT in combination with either delayed SPECT or delayed planar imaging has been found to be far superior to dual-phase planar imaging or SPECT. Major advantages of SPECT/CT include its ability to differentiate inferior from inferior-posterior glands by combining the three-dimensional functional information of SPECT with the anatomical information of CT [8].

Although SPECT/CT may be a viable non-operating room alternative in locating an ectopic parathyroid adenoma, the use of gamma probe cameras during thoroscopic surgery allows more accurate unilateral neck exploration, decreased operative time, decreased morbidity, and improved patient care [6].

Case Report

A 34-year-old man was diagnosed with hypertension and hypercalcemia. He denied any symptoms of chest pain, shortness of breath, nausea, vomiting, diarrhea, palpitations, or headache. He also denied any history of nephrolithiasis and any bone fractures or bone pain. The

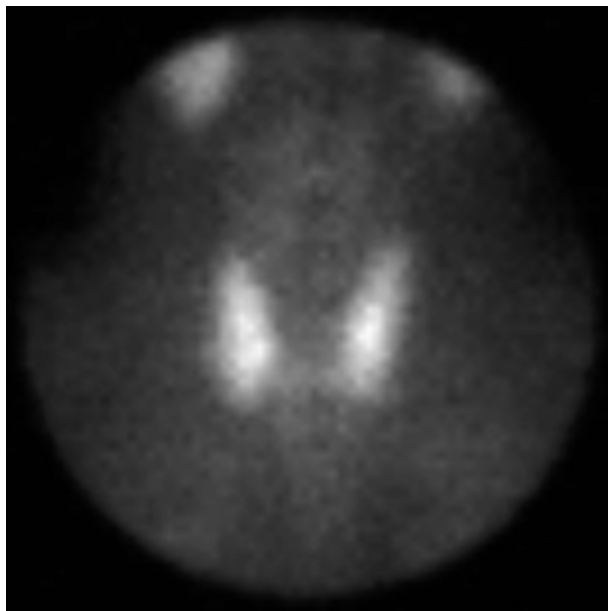


Figure 1A. 35-year-old man with hypertension and hypercalcemia. Tc-99m sestamibi scan shows no uptake in the neck.

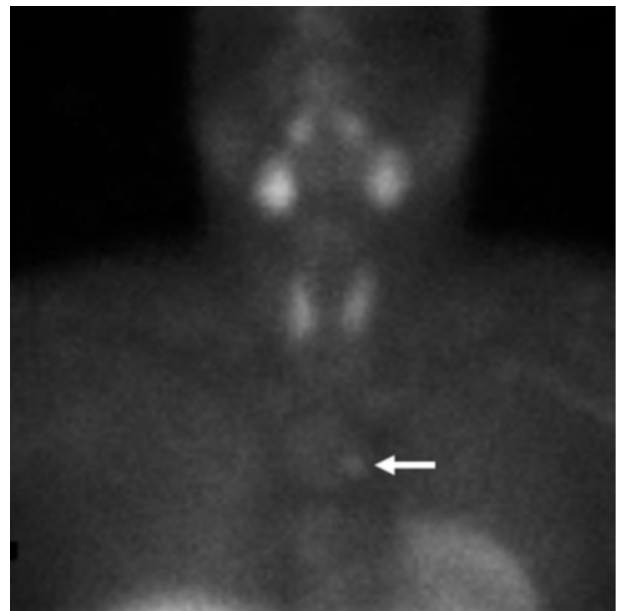


Figure 1B. Tc-99m sestamibi scan shows increased uptake in the upper mediastinum (arrow).

patient had a sestamibi scan with 740 mBq (20 mCi) Tc-99m sestamibi administered intravenously, followed by planar imaging on a dual head gamma camera (Millennium MG, General Electric, Milwaukee, WI) of the neck and chest after a delay of 20 minutes and repeated after 2 hours. This scan demonstrated no evidence of abnormal uptake in the neck (Fig. 1A) and demonstrated increased uptake in the upper mediastinum (Fig. 1B). A chest CT without intravenous contrast was acquired on a multidetector General Electric CT scanner, which demonstrated a 7mm density in the superior mediastinum adjacent to the aortic arch slightly anterior and to the right of the trachea which was thought to represent the aberrant parathyroid adenoma (Fig. 2A). The patient was advised that surgery would be needed for removal of this parathyroid adenoma.

The patient returned to the hospital for elective excision of the parathyroid adenoma approximately three months later. During the interim, he denied any symptoms of hypercalcemia and continued to take his previously prescribed antihypertensive medication. Physical exam prior to the day of surgery was unremarkable including no palpable lymph nodes and no palpable neck mass. His ionized calcium level prior to the day of surgery was elevated at 1.36 mmol/L (normal range 1.15-1.29) with a previous total calcium level elevated at 11.1 mg/dL (normal range 8.6-10 mg/dL), alkaline phosphatase normal at 88 u/L (normal range 30-125 u/L) and albumin normal at 4.7 g/dL (normal range 4.0-5.0 g/dL).

On the day of the elective surgery, to aid gamma probe

detection of an ectopic parathyroid adenoma, the patient received an intravenous injection of 12.3 mCi of Tc99m-sestamibi approximately one hour prior to surgery. In addition, to help provide an alternative means of localization, the patient was also injected intraoperatively with 1% methylene blue (10 mg/ml) 95 ml with 0.9% NaCl 500 ml intravenously. A partial upper sternotomy split was performed with a partial pericardiotomy dissection at the aortic arch. However, no discrete lesion was visualized by the surgeons at this time. The gamma probe localized increased uptake in the left half of the thymus with associated discrete nodularity. This area was excised and sent to pathology. No blue dye activity was seen in this tissue. The frozen section received by the pathologist was confirmed to be hypercellular parathyroid. No uptake was detected by the gamma probe at the aortic arch. The left thymus was resected with the associated thymic lesion which had increased uptake seen with gamma probe utilization. The final pathology report confirmed this resected left region of the thymus measuring approximately 5 mm x 4 mm x 4 mm as hypercellular parathyroid consistent with parathyroid adenoma.

The patient's open sternotomy was sutured with placement of a mediastinal drain and he was taken to recovery without complications. His subsequent ionized calcium levels were 0.92 mmol/L, 0.89 mmol/L, 1.29 mmol/L (normal range 1.15-1.29 mmol/L) with a total calcium of 8.5 mg/dL (normal range 8.6-10.0 mg/dL). The patient did not have any hypocalcemic symptoms including a negative Chvostek's sign, a negative Trousseau's sign, no hyperreflexia, and no tetany. The patient recovered well and the mediastinal drain was removed prior to discharge. He was sent home one day after surgery with a prescription for calcium carbonate 500 mg, one tablet three times daily, and pain management with Percocet as needed.



Figure 2A. Chest CT without intravenous contrast shows a 7 mm density in the superior mediastinum adjacent to the aortic arch slightly anterior and to the right of the trachea consistent with an ectopic parathyroid adenoma (arrow). This lesion was subsequently determined to be a lymph node.

Discussion

The use of an intraoperative gamma probe in the localization of the ectopic parathyroid adenoma has been shown to be very useful. The previous neck exploration required for parathyroidectomy involved a bilateral exploration starting from the bifurcation of the inferior thyroid artery, back to the thyroid lobe, in the retropharyngeal and

thyo-carotid spaces, into the thymus and upper mediastinum and behind the trachea and esophagus [9]. The available preoperative localization tools such as ultrasound, CT, and MRI have a diagnostic accuracy of 57-68% dependent on the size and location of the pathologic parathyroid tissue [6]. Now, not only is surgical time considerably reduced with the aid of the gamma probe for localization but there is a considerable reduction in the morbidity and surgical complications associated with neck exploration and nonvisualization of the solitary ectopic adenoma. Average operative time to remove parathyroid disease was 80 minutes of which 20-40 minutes was from waiting for frozen section results [10].

In conclusion, the intraoperative gamma probe was used to successfully identify an occult ectopic parathyroid adenoma. Pre-operative CT scan suggested the possibility of an ectopic parathyroid adenoma deep in the mediastinum, adjacent to major vessels, the exploration of which could have led to unnecessary morbidity without any benefit to the patient. However, gamma probe localization led to successful exploration of otherwise subtle small ectopic adenoma embedded within the thymus which only retrospectively was seen on the axial CT image measuring approximately 5 mm x 3.5 mm (Fig. 2B). The lesion to the right of trachea that was originally thought to be the aberrant parathyroid adenoma was likely a reactive lymph node.

The use of the intraoperative gamma probe provides a distinct advantage over conventional techniques by significantly reducing surgical time and reducing the morbidity and/or complications associated with surgical exploration. In the future, in addition to obtaining intraoperative calcium levels, the intraoperative gamma probe can also be used in order to ensure complete removal of an occult ectopic parathyroid adenoma without undue risk to the patient.

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Figure 2B. Chest CT without intravenous contrast shows a small ectopic adenoma embedded within the thymus which only retrospectively was seen on the axial CT image measuring approximately 5 mm x 3.5 mm (arrow).

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